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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,746	04/03/2001	Hans J. Hansen	018733-1015	1224

22428 7590 04/07/2004

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EXAMINER

SAUNDERS, DAVID A

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

823,746

Applicant(s)

HANSEN et al

Examiner

SAUNDERS

Group Art Unit

1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 1/6/04
- ☒ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 1-9, 18-27, 30-36, 38-43, 45-67 is/are pending in the application.
Of the above claim(s) 53-56 is/are withdrawn from consideration.
- ☒ Claim(s) 1-9, 19-24, 30-34, 36, 38-41, 43, 45-47 is/are allowed.
- ☒ Claim(s) 18, 26-27, 35, 42, 48-52, 57-62 is/are rejected.
- ☒ Claim(s) 25 is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____.
 - ☐ received in this national stage application from the International Bureau (PCT Rule 1.7.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ ☐ Interview Summary, PTO-413
- ☒ Notice of Reference(s) Cited, PTO-892 ☐ Notice of Informal Patent Application, PTO-152
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948 ☐ Other _____

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Amendment of 1/6/04 has been entered. Claims 1-9, 18-27, 30-36, 38-43, 45-67 are pending. Claims 53-56 remain withdrawn.

It is noted that Figures 1-7 contain polypeptide and polynucleotide sequences. Fill compliance with 37 CFR 1.821-1.825 is required.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Except as noted infra, applicant's amendment and urgings have overcome previously stated rejections under 35 USC 112, first and second paragraphs.

Claims 48-52 and 57-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 48, 52, 57 and 61-63 Markush group members (d) and (e) are indefinite because it is not clear what the squiggly bond between "NH" and "D-ala" represents. Applicant's response (pg.24) has argued that one of skill would understand this is the "bond between the thiourea moiety and the rest of the peptide" and that the "NH" is "from the amino terminus of the D-Ala moiety." If this is so why is not the "NH" of the D-Ala moiety merely connected thereto by a conventional, straight-lined bond? The examiner remains confused as to whether there are other moieties (e.g. an [^]oligopeptide of unspecified nature) between the thiourea and the D-Ala moieties. The specification has given no guidance.

Applicant's amendment has necessitated the following new grounds of rejection under 35 USC 112.

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Claims 18, 26-27, 35, 42 and 67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 depends from cancelled claim 16.

Claim 26 is utterly confusing by reciting that the "arm that specifically binds a targeted tissue is...mAb 679." Note that base claim 1 has stated that the "arm that specifically binds a targetable conjugate...comprises the F_U of mAb 679." This same mAb cannot bind to both the targeted tissue and the targetable conjugate. It is believed that the latter recites the correct binding specificity of mAb 679 (specification page 37).

If one assumes that recitation of "mAb 679" in claim 26 is correct then, claim 26 would remain confusing by reciting (lines 2 and 3) "human". The examiner understands mAb 679 to be of murine origin; thus, it cannot be of human origin and still be "mAb 679", since even a human antibody against the same epitope would have human, rather than murine, CDR sequences.

Claim 27 is confusing by reciting "human" and "chimeric". Since claim 1 has limited the "arm that binds a targetable conjugate" to "mAb 679" (which is deemed to be of murine origin), recitation of "human" is confusing, for reasons noted regarding claim 26 supra. Also claim 1 has limited this "arm" to an F_U; thus it makes no sense to refer to this as "chimeric" (see examiner's rejection of claims 34, 36-37 and 41 in previous action at page 5).

In claim 35 recitation of "human" is confusing. As noted supra regarding claim 26, it is considered that "human" does not properly describe the "679" component of

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claim 35. Likewise, the examiner considers that the Mv-9 component of claim 35 is of murine origin and thus cannot be properly described as "human."

Claim 42 is confusing for the same reasons stated supra for claim 35. It is considered that term "human" cannot be properly applied to either the "679" or the "MN-14" components of claim 42.

Claims 35 and 42 are confusing by each reciting "and/or" and later "and" between the recited pairs of MAbs.

New claim 67 is confusing in part (c), line 3 there of by reciting "at least one epitope". Is this "epitope" the one that is recognized by the "other arm" component of part (A).

Claim 25 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. By reciting "other arm that specifically binds a targetable conjugate is a monoclonal antibody or fragment...", claim 25 fails to limit base claim 1, which requires this "other arm" to be the "F_U of mAb 679." The "mAb 679" is inherently a monoclonal antibody, and "F_U" is inherently a fragment thereof.

Applicant's amendment of claim 1 has overcome previous prior art rejections of claim 1 and its dependents based upon Barbet et al alone or in view of secondary references.

A new prior art rejection follows:

Claim 67 is rejected under 35 U.S.C. 103(a) as being unpatentable over Barbet et al (5,274,076) in view of Bagshawe et al (5,683,694).

Teachings of Barbet et al with respect to use of bispecific antibodies having i) one arm directed against a targeted tissue/cell and ii) another arm directed against HSG, which arm thus serves to bind a conjugate molecule having i) two HSG moieties and ii) an effector ~~or~~ for imaging moiety.

Barbet et al. Teach a method in accord with instant claim 67 (page 6, lines 38-55) except for the facts that they do not specifically teach an enzyme as the therapeutic agent on the conjugate, and that they do not teach prodrugs.

Bagshawe et al. show that it is known to employ bispecific antibodies, with one arm directed to a target antigen on a cell and a second arm directed to an enzyme, in a therapeutic method. The enzyme in such case converts a prodrug to an active drug at the site where the bispecific antibody has bound to antigen. See col.2, lines 49-58.

Since Bagshawe et al. show that an enzyme that activates a prodrug is known to fall within the armamentarium of therapeutic agents that can be targeted by bispecific antibodies, it would have been obvious to provide the enzyme of Bagshawe et al. conjugated to a hapten/epitope recognized by the antibody in the second arm of the bispecific antibodies of Barbet et al. The examiner considers that the lack of teaching of prodrug activating enzymes as being among the therapeutic agents listed by Barbet et al. arises from the fact that prodrug activating enzymes were not well established as therapeutic agents at the time that Barbet et al. filed, rather than from any consideration that such enzymes would not be compatible with their taught targeting methods.

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The examiner considers that the combination of references is proper, since the cytotoxic drugs produced by the enzyme component of Bagshawe et al. correspond to the cytotoxic drugs taught by Barbet et al. (col.5, lines 16-24). Further, one would have fully expected that conjugates of hapten and enzyme would retain their prodrug activating function, because it has been conventional to provide conjugates of enzymes to other molecules, with a retention of enzymatic activity. See Bagshawe et al. at col.2, lines 34-48 and at col.7, line 56-col.8, line 59 regarding antibody-enzyme conjugates, for example.

This application contains claims 53-56 are drawn to an invention nonelected with traverse in Paper No. 5. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. The examiner can normally be reached on Monday-Thursday from 8:00a.m to 5:30p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Saunders/tgd

April 2, 2004


DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182-1644